REMARKS

Upon entry of this amendment, claims 1-3, 5 and 10-11 are pending in the instant application. Claims 1-3, and 5 have been amended and claims 10 and 11 have been added. Claims 4, and 6-9 have been cancelled as drawn to a non-elected invention. Applicants reserve the right to pursue the subject matter of these claims in a continuing application. Support for new claim 10 is found at least at page 12. Support for new claim and 11 and amended claims presented herein can be found at least at page 17 and throughout the specification and the claims as originally filed. Accordingly, no new matter has been added.

I. CLAIM REJECTION

Claims 1-3 are objected to because of the following informalities: in claims 1-3, Applicants employ the use of "(....)" and "{....}". The Examiner requested that these should be deleted and replaced with the appropriate punctuation. Applicants have amended claims 1-3 to correct the punctuation and respectfully request that the rejection be withdrawn.

II. CLAIM REJECTION UNDER 35 U.S.C. §102

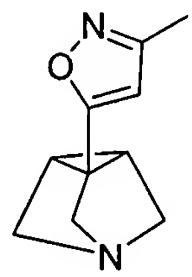
The Examiner rejected claims 1-3, and 5 under 35 U.S.C. 102(b) as being anticipated by WO 92/11261 to Macleod ("Macleod"). The Examiner states "Macleod et al. disclose a method of treating glaucoma by administering to a person in need thereof an effective amount of the compound in Example 6, where the "Het" is isoxazole substituted with a cycloalkyl and 6-membered heterocyclic groups (as represented by the fused rings), and Y is methyl." *See*, Office Action at page 3. Applicants traverse the rejection as it applies to the pending claims as amended herein.

Applicants respectfully note that in Example 6, Macleod does not disclose an isoxazole substituted with a cycloalkyl and a 6-membered ring, but rather Macleod discloses an isoxazole substituted with an alkyl group (methyl) and a 7-membered ring, azatricyclo[2.2.1.$0^{2,6}$]heptane.

Macleod teaches a class of substituted azatricyclic compounds that may be useful in lowering intraocular pressure, thereby treating glaucoma. *See*, Macleod, page 1. The Macleod compounds all contain the core structure, 4-azatricyclo[2.2.1.$0^{2,6}$]heptane. The core azatricyclic structure found in the Macleod compounds can be substituted with a variety of different

substituents such as an amide, ester, oxime, ether, or a heterocyclic ring system. Several heterocyclic ring systems are described as suitable substituents in Macleod, including oxadiazole, thiadiazole, oxathiazole, isothiazole, oxazole, thiazole, as well as isoxazole.

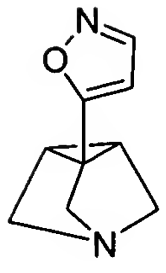
Macleod lists several different species of substituted azatricyclic compounds. In one example, Example 6, 1-[5-(3-methylisoxazol)-yl]-4-azatricyclo[2.2.1.$0^{2,6}$]heptane, is disclosed. This compound is an azatricyclo[2.2.1.$0^{2,6}$]heptane substituted with a (3-methyl) isoxazole:



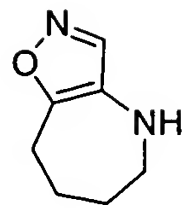
Example 6

The claimed invention relates to lowering intraocular pressure, thereby treating glaucoma, using substituted isoxazole compounds. The isoxazole compounds used in the claimed invention are optionally substituted with one or more substituents. However, none of the claimed substituents is an azatricyclic moiety. Isoxazoles which contain fused substituents are described in claim 1, parts b 2-5. However, none of the singly attached substituents described in claim 1, part b 1, is a *non-aromatic heterocycle*, let alone a 4-azatricyclo[2.2.1.$0^{2,6}$]heptane ring.

Claim 1, part b 5, of the instant invention relates to an isoxazole where two adjacent substituents form a non-aromatic heterocycle that is fused to the isoxazole. These fused isoxazoles differ from isoxazoles with non-fused substituents. In general, compounds that contain fused rings are structurally distinct from compounds with non-fused substituents, because fused rings restrict conformation of the bicyclic system and prohibit rotation of the substituents, therefore, creating a more rigid structure. Substituents that are not fused are allowed to rotate freely and result in a more flexible structure. The isoxazoles fused to other rings described in claim 1 parts b 2-5 are structurally unlike isoxazoles with non-fused substituents. Compare an azatricyclo[2.2.1.$0^{2,6}$]heptane substituted with an isoxazole with an azacycloheptane fused with an isoxazole:



Non-fused heterocyclic substituent



Fused heterocyclic substituent

Macleod does not teach or suggest compounds that do not contain an azatricyclic moiety. Such compounds are not encompassed by the instant invention. Thus, because Macleod does not teach or suggest all of the limitations of the claimed invention, Applicants assert that claim 1, as amended herein (and 2-3, 5, 10and 11, which depend therefrom) are not anticipated by Macleod. Therefore, Applicants respectfully request reconsideration and withdrawal of the present rejection.

CONCLUSION

On the basis of the foregoing amendments, Applicants respectfully submit that the pending claims are in condition for allowance. If there are any questions regarding these amendments and remarks, the Examiner is encouraged to contact the undersigned at the telephone number provided below.

Respectfully submitted,

Reg No. 45,409

Ivor R. Elrifi, Esq., Reg. No. 39,529
Attorney for Applicant(s)
c/o MINTZ, LEVIN
Tel: (617) 542-6000
Fax: (617) 542-2241
Customer No.: 30623

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